09/993,290
Search LYook
1/25/05

d his

(FILE 'HOME' ENTERED AT 17:05:50 ON 25 JAN 2005)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 17:06:05 ON 25 JAN 2005

L1 26 S (COMPLEMENT C3) AND (INSULIN RESISTANCE)
L2 16 DUPLICATE REMOVE L1 (10 DUPLICATES REMOVED)
L3 4 S L2 AND MARKER?

=>

```
d his

     (FILE 'HOME' ENTERED AT 17:05:50 ON 25 JAN 2005)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
     17:06:05 ON 25 JAN 2005
L1            26 S (COMPLEMENT C3) AND (INSULIN RESISTANCE)
L2            16 DUPLICATE REMOVE L1 (10 DUPLICATES REMOVED)
L3             4 S L2 AND MARKER?

=>
```

```
d his

     (FILE 'HOME' ENTERED AT 17:05:50 ON 25 JAN 2005)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
     17:06:05 ON 25 JAN 2005
L1            26 S (COMPLEMENT C3) AND (INSULIN RESISTANCE)
L2            16 DUPLICATE REMOVE L1 (10 DUPLICATES REMOVED)
L3             4 S L2 AND MARKER?

=>
```

```
d his

     (FILE 'HOME' ENTERED AT 17:05:50 ON 25 JAN 2005)

     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT
     17:06:05 ON 25 JAN 2005
L1            26 S (COMPLEMENT C3) AND (INSULIN RESISTANCE)
L2            16 DUPLICATE REMOVE L1 (10 DUPLICATES REMOVED)
L3             4 S L2 AND MARKER?

=>
```

ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:708363 CAPLUS
DN 141:329868
ED Entered STN: 31 Aug 2004
TI Inflammation, **insulin resistance**, and adiposity: A study of first-degree relatives of type 2 diabetic subjects
AU Kriketos, Adamandia D.; Greenfield, Jerry R.; Peake, Phil W.; Furler, Stuart M.; Denyer, Gareth S.; Charlesworth, John A.; Campbell, Lesley V.
CS Diabetes and Obesity Research Program, Garvan Institute of Medical Research, Sydney, Australia
SO Diabetes Care (2004), 27(8), 2033-2040
CODEN: DICAD2; ISSN: 0149-5992
PB American Diabetes Association, Inc.
DT Journal
LA English
CC 14-8 (Mammalian Pathological Biochemistry)
AB OBJECTIVE - Inflammatory **markers** such as C-reactive protein (CRP) are associated with **insulin resistance**, adiposity, and type 2 diabetes. Whether inflammation causes **insulin resistance** or is an epiphenomenon of obesity remains unresolved. We aimed to determine whether first-degree relatives of type 2 diabetic subjects differ in insulin sensitivity from control subjects without a family history of diabetes, whether first-degree relatives of type 2 diabetic subjects and control subjects differ in CRP, adiponectin, and complement levels, and whether CRP is related to insulin sensitivity independently of adiposity. RESEARCH DESIGN AND METHODS - We studied 19 young normoglycemic nonobese first-degree relatives of type 2 diabetic subjects and 22 control subjects who were similar for age, sex, and BMI. Insulin sensitivity (glucose infusion rate [GIR]) was measured by the euglycemic-hyperinsulinemic clamp. Dual-energy x-ray absorptiometry determined total and abdominal adiposity. Magnetic resonance imaging measured abdominal adipose tissue vols. RESULTS - First-degree relatives of type 2 diabetic subjects had a 20% lower GIR than the control group (51.8±3.9 vs. 64.9±4.6 μmol · min-1 · kg fat-free mass-1, P = 0.04). However, first-degree relatives of subjects with type 2 diabetes and those without a family history of diabetes had normal and comparable levels of CRP, adiponectin, and complement proteins. When the cohort was examined as a whole, CRP was inversely related to GIR (r = -0.33, P = 0.04) and adiponectin (r = -0.34, P = 0.03) and pos. related to adiposity (P < 0.04). However, CRP was not related to GIR independently of fat mass. In contrast to C3 (r = 0.41, P = 0.009) and factor B (r = 0.43, P = 0.005), CRP was unrelated to factor D. CONCLUSIONS - The insulin-resistant state is not associated with changes in inflammatory **markers** or complement proteins in subjects at high risk of type 2 diabetes. Our study confirms a strong relationship between CRP and fat mass. Increasing adiposity and **insulin resistance** may interact to raise CRP levels.
ST inflammation **insulin resistance** adiponectin adiposity diabetes risk; adiponectin C reactive protein diabetes
IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(C-reactive, inflammatory **marker**; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
IT Cytokines
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(adiponectin; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
IT Biomarkers (biological responses)
Human
Obesity
Risk assessment

(inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
IT Diabetes mellitus
(non-insulin-dependent; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
IT 80295-32-5, Complement C1 80295-41-6, **Complement C3**
80295-48-3, Complement C4
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

(1) Brull, D; Atherosclerosis 2003, V168, P192
(2) Campos, S; Mol Cell Biol 1992, V12, P1789 CAPLUS
(3) Carey, D; Diabetes 1996, V45, P633 CAPLUS
(4) Crook, M; Diabet Med 2004, V21, P203 CAPLUS
(5) Dandona, P; Am J Cardiol 2002, V90(Suppl 5), P27G
(6) DeFronzo, R; Am J Physiol 1979, V237, PE214 CAPLUS
(7) Duncan, B; Diabetes 2003, V52, P1799 CAPLUS
(8) Eriksson, J; N Engl J Med 1989, V321, P337 MEDLINE
(9) Festa, A; Circulation 2000, V102, P42 MEDLINE
(10) Festa, A; Diabetes 2002, V51, P1131 CAPLUS
(11) Furler, S; Obes Res 2001, V9, P535 CAPLUS
(12) Gan, S; Diabetes 2002, V51, P3163 CAPLUS
(13) Greenfield, J; Circulation 2004, V109, P3022 CAPLUS
(14) Griselli, M; J Exp Med 1999, V190, P1733 CAPLUS
(15) Haffner, S; Am J Cardiol 2003, V92(Suppl 4), P18J
(16) Haffner, S; Diabetes Care 2003, V26, P2796 CAPLUS
(17) Hak, A; Arterioscler Thromb Vasc Biol 1999, V19, P1986 CAPLUS
(18) Han, T; Diabetes Care 2002, V25, P2016 CAPLUS
(19) Hu, F; Diabetes 2004, V53, P693 CAPLUS
(20) Jenkins, A; Twin Res 2000, V3, P148 MEDLINE
(21) Kiechl, S; N Engl J Med 2002, V347, P185 CAPLUS
(22) Kishore, U; Immunopharmacology 2000, V49, P159 CAPLUS
(23) Kopp, H; Arterioscler Thromb Vasc Biol 2003, V23, P1042 CAPLUS
(24) Krakoff, J; Diabetes Care 2003, V26, P1745 CAPLUS
(25) Kriketos, A; Diabet Med 2003, V20, P294 MEDLINE
(26) Kriketos, A; J Clin Endocrinol Metab 2003, V88, P793 CAPLUS
(27) MacGregor, A; Clin Chem 2004, V50, P130 CAPLUS
(28) Matsumoto, K; Atherosclerosis 2000, V152, P415 CAPLUS
(29) McGarry, J; Diabetes 2002, V51, P7 CAPLUS
(30) McLaughlin, T; Circulation 2002, V106, P2908 CAPLUS
(31) Mohamed-Ali, V; J Clin Endocrinol Metab 1997, V82, P4196 CAPLUS
(32) Nakanishi, S; Diabetes Care 2003, V26, P2754 CAPLUS
(33) Newman, B; Diabetologia 1987, V30, P763 MEDLINE
(34) Ouchi, N; Circulation 2003, V107, P671 CAPLUS
(35) Pajvani, U; J Biol Chem 2003, V278, P9073 CAPLUS
(36) Pannacciulli, N; Int J Obes Relat Metab Disord 2001, V25, P1416 CAPLUS
(37) Pepys, M; J Clin Invest 2003, V111, P1805 CAPLUS
(38) Reaven, G; Diabetes 1988, V37, P1595 MEDLINE
(39) Romano, M; J Clin Endocrinol Metab 2003, V88, P5321 CAPLUS
(40) Rossetti, L; Diabetes Care 1990, V13, P610 MEDLINE
(41) Satoh, N; Diabetes Care 2003, V26, P2493 CAPLUS
(42) Schmidt, M; Lancet 1999, V353, P1649 MEDLINE
(43) Sites, C; Fertil Steril 2002, V77, P128
(44) Snijder, B; Diabetes Care 2003, V26, P1656
(45) Thorand, B; Arch Intern Med 2003, V163, P93 CAPLUS
(46) Volanakis, J; Ann N Y Acad Sci 1982, V389, P235 CAPLUS

(47) Wellen, K; J Clin Invest 2003, V112, P1785 CAPLUS
(48) Weyer, C; J Clin Endocrinol Metab 2001, V86, P1930 CAPLUS
(49) Yamauchi, T; Nature 2003, V423, P762 CAPLUS
(50) Yudkin, J; Arterioscler Thromb Vasc Biol 1999, V19, P972 CAPLUS
(51) Yudkin, J; Diabetologia 2000, V43, P1099 CAPLUS

ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:708363 CAPLUS
DN 141:329868
ED Entered STN: 31 Aug 2004
TI Inflammation, **insulin resistance**, and adiposity: A study of first-degree relatives of type 2 diabetic subjects
AU Kriketos, Adamandia D.; Greenfield, Jerry R.; Peake, Phil W.; Furler, Stuart M.; Denyer, Gareth S.; Charlesworth, John A.; Campbell, Lesley V.
CS Diabetes and Obesity Research Program, Garvan Institute of Medical Research, Sydney, Australia
SO Diabetes Care (2004), 27(8), 2033-2040
CODEN: DICAD2; ISSN: 0149-5992
PB American Diabetes Association, Inc.
DT Journal
LA English
CC 14-8 (Mammalian Pathological Biochemistry)
AB OBJECTIVE - Inflammatory **markers** such as C-reactive protein (CRP) are associated with **insulin resistance**, adiposity, and type 2 diabetes. Whether inflammation causes **insulin resistance** or is an epiphenomenon of obesity remains unresolved. We aimed to determine whether first-degree relatives of type 2 diabetic subjects differ in insulin sensitivity from control subjects without a family history of diabetes, whether first-degree relatives of type 2 diabetic subjects and control subjects differ in CRP, adiponectin, and complement levels, and whether CRP is related to insulin sensitivity independently of adiposity. RESEARCH DESIGN AND METHODS - We studied 19 young normoglycemic nonobese first-degree relatives of type 2 diabetic subjects and 22 control subjects who were similar for age, sex, and BMI. Insulin sensitivity (glucose infusion rate [GIR]) was measured by the euglycemic-hyperinsulinemic clamp. Dual-energy x-ray absorptiometry determined total and abdominal adiposity. Magnetic resonance imaging measured abdominal adipose tissue vols. RESULTS - First-degree relatives of type 2 diabetic subjects had a 20% lower GIR than the control group (51.8±3.9 vs. 64.9±4.6 μmol · min-1 · kg fat-free mass-1, P = 0.04). However, first-degree relatives of subjects with type 2 diabetes and those without a family history of diabetes had normal and comparable levels of CRP, adiponectin, and complement proteins. When the cohort was examined as a whole, CRP was inversely related to GIR (r = -0.33, P = 0.04) and adiponectin (r = -0.34, P = 0.03) and pos. related to adiposity (P < 0.04). However, CRP was not related to GIR independently of fat mass. In contrast to C3 (r = 0.41, P = 0.009) and factor B (r = 0.43, P = 0.005), CRP was unrelated to factor D. CONCLUSIONS - The insulin-resistant state is not associated with changes in inflammatory **markers** or complement proteins in subjects at high risk of type 2 diabetes. Our study confirms a strong relationship between CRP and fat mass. Increasing adiposity and **insulin resistance** may interact to raise CRP levels.
ST inflammation **insulin resistance** adiponectin adiposity diabetes risk; adiponectin C reactive protein diabetes
IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(C-reactive, inflammatory **marker**; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
IT Cytokines
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(adiponectin; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)
IT Biomarkers (biological responses)
Human
Obesity
Risk assessment

(inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)

IT Diabetes mellitus
(non-insulin-dependent; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)

IT 80295-32-5, Complement C1 80295-41-6, **Complement C3**
80295-48-3, Complement C4
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; inflammation, **insulin resistance**, and adiposity in first-degree relatives of type 2 diabetic subjects)

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Brull, D; Atherosclerosis 2003, V168, P192
(2) Campos, S; Mol Cell Biol 1992, V12, P1789 CAPLUS
(3) Carey, D; Diabetes 1996, V45, P633 CAPLUS
(4) Crook, M; Diabet Med 2004, V21, P203 CAPLUS
(5) Dandona, P; Am J Cardiol 2002, V90(Suppl 5), P27G
(6) DeFronzo, R; Am J Physiol 1979, V237, PE214 CAPLUS
(7) Duncan, B; Diabetes 2003, V52, P1799 CAPLUS
(8) Eriksson, J; N Engl J Med 1989, V321, P337 MEDLINE
(9) Festa, A; Circulation 2000, V102, P42 MEDLINE
(10) Festa, A; Diabetes 2002, V51, P1131 CAPLUS
(11) Furler, S; Obes Res 2001, V9, P535 CAPLUS
(12) Gan, S; Diabetes 2002, V51, P3163 CAPLUS
(13) Greenfield, J; Circulation 2004, V109, P3022 CAPLUS
(14) Griselli, M; J Exp Med 1999, V190, P1733 CAPLUS
(15) Haffner, S; Am J Cardiol 2003, V92(Suppl 4), P18J
(16) Haffner, S; Diabetes Care 2003, V26, P2796 CAPLUS
(17) Hak, A; Arterioscler Thromb Vasc Biol 1999, V19, P1986 CAPLUS
(18) Han, T; Diabetes Care 2002, V25, P2016 CAPLUS
(19) Hu, F; Diabetes 2004, V53, P693 CAPLUS
(20) Jenkins, A; Twin Res 2000, V3, P148 MEDLINE
(21) Kiechl, S; N Engl J Med 2002, V347, P185 CAPLUS
(22) Kishore, U; Immunopharmacology 2000, V49, P159 CAPLUS
(23) Kopp, H; Arterioscler Thromb Vasc Biol 2003, V23, P1042 CAPLUS
(24) Krakoff, J; Diabetes Care 2003, V26, P1745 CAPLUS
(25) Kriketos, A; Diabet Med 2003, V20, P294 MEDLINE
(26) Kriketos, A; J Clin Endocrinol Metab 2003, V88, P793 CAPLUS
(27) MacGregor, A; Clin Chem 2004, V50, P130 CAPLUS
(28) Matsumoto, K; Atherosclerosis 2000, V152, P415 CAPLUS
(29) McGarry, J; Diabetes 2002, V51, P7 CAPLUS
(30) McLaughlin, T; Circulation 2002, V106, P2908 CAPLUS
(31) Mohamed-Ali, V; J Clin Endocrinol Metab 1997, V82, P4196 CAPLUS
(32) Nakanishi, S; Diabetes Care 2003, V26, P2754 CAPLUS
(33) Newman, B; Diabetologia 1987, V30, P763 MEDLINE
(34) Ouchi, N; Circulation 2003, V107, P671 CAPLUS
(35) Pajvani, U; J Biol Chem 2003, V278, P9073 CAPLUS
(36) Pannacciulli, N; Int J Obes Relat Metab Disord 2001, V25, P1416 CAPLUS
(37) Pepys, M; J Clin Invest 2003, V111, P1805 CAPLUS
(38) Reaven, G; Diabetes 1988, V37, P1595 MEDLINE
(39) Romano, M; J Clin Endocrinol Metab 2003, V88, P5321 CAPLUS
(40) Rossetti, L; Diabetes Care 1990, V13, P610 MEDLINE
(41) Satoh, N; Diabetes Care 2003, V26, P2493 CAPLUS
(42) Schmidt, M; Lancet 1999, V353, P1649 MEDLINE
(43) Sites, C; Fertil Steril 2002, V77, P128
(44) Snijder, B; Diabetes Care 2003, V26, P1656
(45) Thorand, B; Arch Intern Med 2003, V163, P93 CAPLUS
(46) Volanakis, J; Ann N Y Acad Sci 1982, V389, P235 CAPLUS

(47) Wellen, K; J Clin Invest 2003, V112, P1785 CAPLUS
(48) Weyer, C; J Clin Endocrinol Metab 2001, V86, P1930 CAPLUS
(49) Yamauchi, T; Nature 2003, V423, P762 CAPLUS
(50) Yudkin, J; Arterioscler Thromb Vasc Biol 1999, V19, P972 CAPLUS
(51) Yudkin, J; Diabetologia 2000, V43, P1099 CAPLUS